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How Does Ethanol Affect the Stability of Simple Model Yeast Membranes?
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Biofuels such as biomass-based ethanol (EtOH) have become increasingly popular as a source of renewable energy, but the higher cost of production and lower energy content make the fuel difficult to compete with petroleum gasoline. Cellulosic biomass can be used to produce bioethanol, but process efficiency is limited by ethanol's cytotoxic nature. One proposed mechanism for EtOH inhibition of yield growth suggests that ethanol diffuses through cell membranes, decreasing the lipid bilayer stability. Bilayers comprising various molar concentrations of 1-palmitoyl-2-oleoylphosphatidlyserine (POPS), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanolamine (POPE), and 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) lipids were simulated using molecular dynamics. Pure POPS, pure POPE, pure POPC, and mixed 30/70 POPS/POPE lipid bilayers were constructed using the CHARMM36 lipid force field. Each lipid bilayer was exposed to molar concentrations of 0.5%, 1%, 2%, 3%, and 4% ethanol EtOH with additional molar concentrations of 5% and 10% EtOH for pure bilayers only. Average bilayer surface area, NMR deuterium order parameters (S_{CD}), and electron density profiles (EDP) were analyzed to interpret bilayer stability. Each analysis indicated decreased membrane stability with increased EtOH concentration, supporting the proposed mechanism. Trends between different lipid bilayer compositions were all similar. Surface area increases resulted from more frequent EtOH bilayer penetrations into the hydrophobic core, causing bilateral expansion of the membrane's walls. S_{CD} values decreased as more EtOH penetrated the bilayer due to the disruption of lipid packing, increasing membrane fluidity and decreasing stabilizing interactions between hydrophobic lipid tails. As overall EtOH concentration increased, EDP plots indicated increased EtOH concentration within the bilayer, past the hydrophilic head region. EDP plots also indicated decreased bilayer thickness. Increased concentration of EtOH within the bilayer is in accordance with S_{CD} results and decreased bilayer thickness supports increased bilayer surface area results.

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Novel Experimental Methods to Resolve Nanoscale Membrane Organizaion and Curvature
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The structures and functions of cell membranes are regulated by their diverse compositions, distinctive intermolecular interactions, and dynamic lateral organization. In particular, the combination of nanoscale membrane curvature and lateral organization of membrane components play a driving force in the initiation and regulation of intricate cellular processes such as endocytosis and exocytosis. However, many hypotheses concerning the nanoscale lipid redistribution in response to curvature are unanswered due to the diffraction limit of current optical imaging techniques. We aim to resolve nanoscale membrane curvature and the redistribution of proteins and lipids phase separated into liquid domains by inducing nanoscale curvature on giant unilamellar vesicles and novel microcopy methods. We achieve this through polarized total internal reflection fluorescence localization microscopy to yield sub-diffraction-limited resolution of membrane curvature and molecular organization. Polystyrene nanoparticles melted into agarose hydrogel substrates create a nanoengineered surface with small curved regions with controlled radii of curvature from 20 nm to 2 μm. These substrates work well with the evanescent field for total internal reflection microscopy because they are thin (<40 nm thick) and have a low index of refraction (<1.4). Micropipette aspiration techniques coupled with nanoengineered substrates enable dynamic control of membrane curvature and noticeable differences in lipid domain appearances. Preliminary data shows that when the vesicle is pressed against a surface, vesicles with coexisting liquid--order and liquid-disorder phases demonstrate an increased propensity for the liquid-disordered phase to localize at the curved regions. Having the capability to resolve these previously irresolvable details allows us to better understand membrane dynamics and molecular sorting, in addition to exploring vital biological and disease related processes that are sensitive to membrane curvature.

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Membrane Curvature - the Assembler of Proteins
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Many biological phenomena require the membrane to change its shape. This process is often mediated by curvature-generating proteins, such as those containing one of many BAR domains. At the same time, membrane curvature controls the way proteins interact with one another and so it acts as a vital signaling mechanism in the cell. We combine theoretical modeling with experimental biophysical methods to study the driving force underlying the reshaping of biological membranes induced by BAR proteins. In particular, we employ a combination of coarse-grained molecular dynamics with field-theoretical simulation methods to study the assembly of proteins on the membrane at molecular resolution. This approach allows us to study how protein-lipid interactions couple with membrane's large-scale morphology. It also lets us identify a surprising sensitivity of protein-protein attractions on key physical membrane properties. On the other hand, by using quantitative fluorescence and atomic force microscopies, we elucidate the curvature-function relationship of membranes at much larger time and length scales. We study the recruitment of BAR proteins on highly curved membranes and how this type of curvature drives the formation of protein scaffolds. We measure the way protein assemblies impact the mechanical properties of membranes and how such effect may lead either to stabilization of complex geometries or the breakage of membrane topology, i.e. scission. Our combined theoretical and experimental approach gives vital clues on the two-way relationship between the assembly of proteins and membrane's mechanical properties and how it may regulate the dynamics in living cells.

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Bin/Amphiphysin/Rvs (BAR) Family Members Bend Membranes in Cells
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We provide direct evidence that Bin/Amphiphysin/Rvs (BAR) family members bend the steady state membrane architecture of organelles in intact cells. In response to inducible BAR molecular actuators, organelles exhibit distinct changes to the orientation and degree of their membrane curvature. This rapidly inducible system may offer a mechanism by which to better understand the structure-function relationship of intracellular organelles.

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Curvature-Generating Proteins and Subcellular Pattern Formation
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Ordered assembly of cellular processes in the form of oscillations and waves is an emerging theme in living cells. Occurrences of such patterns indicate the presence of local and global coupling mechanisms. However, the nature of the coupling remains to be determined. In our recent work, we discovered a striking appearance of FBP17, one of the Bin1/amphiphysin/Rvs167 (BAR) domain proteins, in actin waves of stimulated mast cells. In addition to being a reporter, FBP17 is essential for wave formation. BAR domain proteins are widely known for their curvature sensing and inducing capabilities, motivating us to directly visualize membrane shape and test its function. We will discuss our findings on the role of physical parameters such as membrane curvature and plasma membrane tension in the propagation of waves. Collectively, our work suggests a mechanochemical basis for pattern formation, which regulates the dynamic reorganization of cell cortex in response to external stimulation, the first and essential step of cellular activation.

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Finely-Fabricated Nanomaterials to Reveal Curvature Roles in Neuronal Network Formation
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In the vertebrate central nervous system, exploratory filopodia transiently form on dendritic branches to sample the neuronal environment and initiate new trans-neuronal contacts. While much is known about the molecules that control filopodia extension and subsequent maturation into functional synapses, the mechanisms that regulate initiation of these dynamic, actin-rich structures have remained elusive.
Using nanomaterials that deform the plasma membrane of neurons, correlative light-electron microscopy (CLEM) and quantitative live cell microscopy, we find that filopodia initiation is suppressed by recruitment of ArhGAP44 to actin-patches that seed filopodia in dendritic branches. Recruitment is mediated by binding of a membrane curvature-sensing ArhGAP44 N-BAR domain to convoluted plasma membrane sections that were deformed inward by actomyosin mediated contractile forces. A GAP domain in the enriched ArhGAP44